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Antiparasitics against ectoparasites in small animals– important pharmaceutical substances or underestimated environmental hazards?

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ABSTRACT

Application of chemical compounds for the control and prevention of arthropod infestations is standard in small animal veterinary medicine. However, concerns about potential negative effects of such substances in the environment, including their circulation in water, soil or plants, and consequent impacts, including infertility or death of sensitive non-target organisms, such as bird, fish, and insects, in particular pollinators, are increasing. Factors that determine the risk of environmental harm from different chemicals are not only their release, but also their retention, bioavailability, degradation, accumulation in different environmental compartments, bioaccumulation in different organisms or their organs, and the effects of excipients commonly used in drug formulations vs. not medical or veterinary use of chemicals. Here we briefly review the substance classes of insecticides, acaricides, or repellents used in veterinary medicine, their effects and possible side effects, and their fate in the environment, including reports of undesirable environmental impacts. In addition to existing literature, the possibilities of preventing, reducing and containing the unwanted release of such chemicals from animal treatments and the pivotal role of experts in veterinary parasitology are discussed. Knowledge gaps concerning the properties of chemicals used for the control of ectoparasites in veterinary medicine that must be addressed in future research are emphasized.

1. Introduction

Antiparasitic compounds (drugs or biocides) play a key role in controlling parasitic infections of domestic animals, and significantly contributed to the admission of dogs and cats to our houses and their roles as companion animals. Currently available registered antiparasitics must be tested for efficacy and safety in experimental and field trials according to pre-determined criteria, and their registration successfully accepted by national or international agencies. Here, we focus on registrations by the European Medicines Agency (EMA) in Europe. This agency provides specific evaluation procedures to support applications for registration (European Medicines Agency, 2025a).

Antiparasitic drugs for veterinary use have been described as (potential) health and environmental hazards, and their application has been criticized in various scientific and popular publications (Mahefarisoa et al., 2021; Wells and Collins, 2022; Dunning, 2023; Tassin de Montaigu et al. 2025). These concerns are particularly directed towards compounds that are effective against arthropods (ectoparasites or vectors). Applications of such compounds on animals mostly relate to prophylaxis against flea, tick, mosquito, or sandfly infestation, and the majority of these compounds are, or have been, also used as insecticides or pesticides in agriculture. Many are considered as (potentially) dangerous to human and animal health and are often associated with lasting undesired effects on "off-target" organisms, such as pollinators that may experience increased mortality and even colony collapses (Dainat et al., 2012; Leska et al., 2021) or fish (as reviewed by Ullah and

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Zorriehzahra, 2015).As pharmaceutical applications on animals can also result in releases of such compounds into the environment, with undesirable consequences, veterinarians must not only consider the consequences of such applications for animal and human health, but also, from the One Health perspective, environmental consequences.

Within the One Health concept, environmental health is a third pillar, complementing human and animal health (Giannelli et al., 2024). Potentially conflicting aims can arise regarding chemoprophylaxis for ectoparasite control in animals: on the one hand, ectoparasites (either as pathogens or vectors of associated diseases) have a serious impact on animal health and welfare, and sometimes human health (Cauvin, 2020); on the other hand, the excretion and dissemination and persistence of chemicals and their unintended toxic effects on non-target animals and humans must be considered in the frame of environmental protection.

In December 2022, the Committee for Veterinary Medicinal Products (CVMP) of the EMA published a reflection paper on the environmental impact of parasite treatments for cats and dogs (European Medicines Agency, 2023), which was open for public consultation until the end of March 2023. It summarized the current state of knowledge about the environmental impacts of cat and dog parasiticides used to protect animals from ectoparasites, and associated vector-borne pathogens. Previously, the use of ectoparasiticides (ectocides) in companion animals (as opposed to farm animals), has been assumed to have a low environmental impact (European Medicines Agency, 2023). A risk-benefit evaluation was clearly recommended by authorities in the UK where imidacloprid and fipronil are banned from agricultural and other outdoor use, but not from veterinary ectocides (Veterinary Medicines Directorate, 2023). In the meantime, the EMA has published a concept paper for the development of a guideline on the methodology to assess environmental risks of ectoparasiticidal products for cats and dogs (European Medicines Agency, 2025b). Owing to the complexity of the topic, the adoption of this guideline by the CVMP is not expected before the end of 2028. In the meantime, the existing knowledge gaps must be filled by scientifically sound evaluations. In this regard, an overlap of the current circulation of environmental contaminants from agriculture and the impact of the same compounds used in small animal veterinary medicine cannot be ignored. Current publications that describe how the halt (or, at least, reduction) of antiparasitic treatment of pets is warranted, claim that detection of pesticides in the environment is due to such treatments (e.g. Teerlink et al., 2017; Tassin de Montaigu et al. 2025). A recent study indicated a substantial contribution of "down-the drain" pathways for fipronil and imidacloprid after spot-on treatment of dogs (Perkins et al., 2024), and insecticide (mostly fipronil/imidacloprid)-contaminated pet hair used by birds as nesting material was recently shown to be linked to decreased breeding success of tits in the UK (Tassin de Montaigu et al. 2025). However, evidence regarding the actual share of veterinary products to environmental contamination is still very weak (Wells and Collins, 2022), and the current discussion neglects major variables in the evaluation of the impact of veterinary products on the environment.

Here we provide an overview of compounds registered as ectocides for dogs and cats, their claims, the current state of knowledge about the environmental hazards they can pose, and suggest a pivotal role for veterinary parasitologists to fill existing knowledge gaps.

2. Definitions

Chemical compounds with a lethal effect on insects (insecticides) or mites and ticks (acaricides) are used in agriculture, but also in households for pest control. The terms "pesticides" and "biocides" overlap and (besides fungicides) also include insecticides and acaricides. By contrast, the term "repellent" describes chemicals that deter infestation with arthropods (also described as "anti-feeding" effect that inhibits blood feeding by hematophagous arthropods which may temporarily infest a host without taking a blood meal). Many products for flea or tick control in pets combine both killing and repelling effects for maximum control. The sale and application of antiparasitic drugs, registered as such under national or European law, are regulated separately from application of biocides to control environmental stages of arthropod pests, including fleas, mosquitoes, flies and others. Biocide application can also require specific permissions, and these can be restricted to qualified persons only (i.e., pest control companies or agencies). Under this legislation, biocides also include repellents to be applied on human skin, such as ethylbutylacetylaminopropionate or diethyltoluamide. Biocides can include chemical insecticides/acaricides, such as pyrethroids or phenothrin, or biological agents such as spore-forming bacteria (European Parliament, Council of the European Union, 1998; Halos et al., 2012; European Chemicals Agency, 2023).

Compounds registered for the use on animals as insecticides, acaricides, and/or repellents are usually considered pharmaceutical substances and are registered as such with EMA. Exceptions are some biocidal compounds, e.g. ethylbutylacetylaminopropionate. Treatment of animals such as horses, not generally exempt from food animal legislation, represent a "gray area" of biocidal application. Beyond synthetic chemicals, biopesticides (naturally occurring substances or microorganisms used to control undesirable microorganisms or arthropods) are becoming increasingly available for pathogen control (European Environment Agency, 2025) and their environmental impact should also be considered (Sullivan et al., 2020). We do not consider these further here, as this is beyond the framework of the topic.

3. Current recommendations for ectoparasite control in cats and dogs

The European Scientific Counsel Companion Animal Parasites® - ESCCAP (2025), as well as other experts groups outside Europe, such as the Companion Animal Parasite Council® - CAPC (2025) and the Tropical Council for Companion Animal Parasites® - TroCCAP (2025), develop and publish guidelines for parasite control in companion animals, including dogs and cats (Dantas-Torres et al., 2020). These guides also include the management of ectoparasites and vector-borne infections (Table 1). In addition, various scientific associations publish guidelines that include vector-control options for control of parasites such as heartworm or *Leishmania*, including a collection of relevant scientific publications on that topic from Europe (European Society of Dirofilariosis and Angiostrongylosis ESDA, 2025; LeishVet (2025); European Advisory Board on Cat Diseases ABCD, 2025).

Although some geographical differences exist, all scientific guidelines commonly recommend treatment upon diagnosis of demodicosis, canine sarcoptosis/feline notoedrosis (mange), and other mite infestations. In contrast, for control of fleas, sandflies, and ticks, regular application of insecticidal/acaricidal and, whenever possible, repelling compounds is recommended for cats and dogs. This treatment aims to prevent transmission of pathogens by these vectors (see Table 1) as well as, in case of fleas, flea allergy dermatitis that can be induced by their saliva (Halliwell et al., 2021).

4. Compound groups and compounds registered against parasitic arthropods of dogs and cats – effects and undesired (side) effects on the environment

Currently, pyrethroids, carbamates, tetracyclic macrolides, neonicotinoids, phenylpyrazoles, organophosphates, semicarbazones, oxadiazines, and, more recently, isoxazolines and bispyrazoles are registered as antiparasitic compounds used as ectocides and/or repellents for use in dogs and/or cats, and piperazines as registered as biocides and formulated for external application on pets (Table 2). With the exception of diazinon (dimpylate), which is used in flea collars, organophosphates are no longer registered for cats and dogs; their use is restricted due to their toxicity in birds (Reece and Handson, 1982). Similarly, the use of amitraz, a formamine derivate, for the control of

Table 1

Overview of important insect- and tick-transmitted pathogens affecting dogs (D) and cats (C) in Europe (ref. Deplazes et al., 2021; European Scientific Counsel Companion Animal Parasites, 2023). Pathogenicity for the mammalian host: + : mild, + +: moderate, + ++ : severe disease. Zoonoses: Y: yes; N: no. Locally or seasonally restricted vectors and associated pathogens are not considered here.

Vector	Pathogen	Host(s)	Pathogenicity	Zoonosis
Fleas: *Ctenocephalides* spp.	*Dipylidium caninum*	D, C	+	Y
	*Acanthocheilonema reconditum**	D	+	N
	Bartonella henselae	D, C	+	Y
	Bartonella vinsonii	D	+ - + ++	N
	Mycoplasma haemofelis	C	+ - + ++	N
	Feline calici virus	C	+ - + ++	N
Sandflies: *Phlebotomus* spp.	*Leishmania infantum, L. donovani**	D, C	+ ++	Y
	Toscana virus and other phleboviruses§§	D	+ - + +	Y
Mosquitoes: Culicidae	*Dirofilaria immitis**	D, C	+ ++	Y
	Dirofilaria repens	D, C	+ - + +	Y
Ticks: Ixodidae		D	+ - + +	Y
Dermacentor reticulatus	*Babesia canis*	D	+ - + ++	N
*Rhipicephalus sanguineus**	*Babesia vogeli**	D	+ - + +	N
	*Hepatozoon canis**	D	+	N
	Acanthocheilonema spp., *Cercopithifilaria* spp.*	D, C	+	N
	*Anaplasma platys**	D	+	N
	*Ehrlichia canis**	D (C)	+ + - + ++	N
	*Rickettsia conorii**	D	+	Y
Ixodes spp§,$	*Babesia microti*-like/*B. vulpes*	D	+ + - + ++	N
	Anaplasma phagocytophilum$	D, C	+ - + +	Y
	Borrelia spp.	D, (C)	+	Y
	Tick-borne encephalitis virus$	D	+ - + ++	Y
Hard ticks§	*Babesia gibsoni* (like)	D	+ - + ++	N
	Cytauxzoon spp.	C	+ - + ++	N
	Francisella tularensis	C	+ - + ++	Y
	Coxiella burnetti	D, C	+	Y

* pathogens/vectors restricted to warmer (Mediterranean and/or southern European) climate zones. For maps on vector distribution see European Center for Disease Prevention and Control (www.ecdc.europa.eu/en/disease-vectors) or European Scientific Counsel Companion Animal Parasites (www.esccap.org/guidelines-maps/)
§different species inferred or vector species unknown
$not common in Southern Europe
§§Dogs are considered as carriers of several zoonotic phleboviruses circulating in Mediterranean Europe; an association between Leishmania infections and virus infections has been shown (e.g. Moriconi et al., 2017; Lelli et al., 2021).

mites in dogs has become increasingly restricted in recent years, because it can be toxic in dogs (specifically diabetes patients) and humans. Additionally, amitraz displays species-specific high toxicity for cats, horses, rodents, and fish, as it forms highly toxic metabolites after preparation of water-based emulsions (Auer et al., 1984; Hugnet et al., 1996, Proudfoot, 2003; Westermann et al. 2004; Gupta and Doss, 2022a; Tosetto Santin et al., 2024). However, amitraz is available in formulations specifically registered for bees (treatment of varroosis) in some countries in Europe.

The most important compounds in each class, their applications in different areas (agriculture, pest control and veterinary medicine) and their effects on humans, animals and the environment are described in the following sections. Where information on the mode of entry into the environment and effects on non-target organisms is known, this is also described.

4.1. Pyrethroids

Deltamethrin, flumethrin, and permethrin are synthetic derivates of pyrethrins, natural insecticides contained in chrysanthemum flowers. Unlike the natural products, pyrethroids exert a longer-lasting and more potent action (Agency for Toxic Substances and Disease Registry, 2003a). In agriculture or as household insecticides, they are used as spray or aerosol bombs, while in human dermatology permethrin is available as an ointment to treat scabies (Cohen, 2020). In small animal veterinary medicine, pyrethroids are mostly formulated in collars or spot-on formulations. Therefore, environmental contamination by spray-drift or runoff from treated surfaces into surface water, the most important entry of these substances, is not connected with veterinary application; rather, wash-off from recently treated dogs that swim in surface waters can result in contamination of water courses. Pyrethroids are usually degraded by sunlight (photolysis) or direct oxidation within one to two days. Because they bind strongly to soil,they usually do not enter groundwater systems and they do not circulate for long before degradation by microorganisms (Singh et al., 2022). Due to this, they also do not circulate in plants and do not volatilize readily from soil surfaces (Agency for Toxic Substances and Disease Registry (US); 2003b). Toxic effects due to irreversible disruption of neuroendocrine activity are most pronounced in fish and other cold-blooded animals (e.g., Decourtye et al., 2004). Therefore, these substances must not be released into water, and manufacturers of antiparasitics/repellents generally recommend that dogs should not be to swim in the first 48 h after spot-on application. Modern collars are formulated in such a way that release of pyrethroids into water is minimized, but swimming can still reduce the efficacy of the collar (European Medicines Agency, 2025c). Toxic effects of pyrethroid differ between type I pyrethroids, such as permethrin, and type II pyrethroids (the latter have an α-cyano moiety); type I pyrethroids induce tremors (T syndrome) while type II induce hyperkinesis (choreoathetosis) and salivation (CS syndrome) and can induce paresthesia after skin contact (Tsuji et al. 2012). Interestingly, cats are much more susceptible to pyrethroid intoxication than dogs. However, a number of pyrethroids are formulated as antiparasitics/repellents for cats as well (Table 2). Mammals excrete pyrethroids quickly after uptake (mostly with urine), but accumulation in fat tissue can occur (Anadón et al., 2009; Singh et al., 2022). Absorption through the skin is < 3 % (Hughes and Edwards, 2010). Toxic effects are acute and related to neurotoxicity, with a variety of clinical signs; chronic toxicity is not relevant since pyrethroids are quickly degraded in the mammalian body (Agency for Toxic Substances and Disease Registry, 2003b).

In the ixodid tick *Rhipicephalus sanguineus*, resistance to permethrin has been reported on several occasions in the Americas (Tian et al., 2023; Arthropod Resistance Database, 2024).

Table 2
Overview on ectocides (substances lethal to ectoparasites, i.e. insecticides and acaricides) and repellents (“anti-feeding” compounds) for the prevention of flea and/or tick infestation in dogs and cats: Chemical compound groups, compounds, and formulations. ACh: acetylcholine; GABA: gamma amino butyric acid. References are given in the text.

Chemical class	Mechanism of action	Compounds for antiparasitic application to pets	Registered formulations
Pyrethroids	Excitotoxicity (inhibition of closure of voltage-gated sodium channels), irreversible due to disruption of neuroendocrine activity; repellent	Deltamethrin, flumethrin, permethrin	Collar (alone or with propoxur or imidacloprid) Spot-on (alone or with imidacloprid, fipronil or dinotefuran) Spray
Tetracyclic macrolides	Permanent Ach receptor activation; binding to chloride channels (contact and ingestion toxicity)	Spinosad	Oral
Carbamates	ACh esterase inhibition (contact toxicity)	Propoxur	Collar (alone or with flumethrin) Shampoo and soap Spray
Neonicotinoides	Modulation of ACh-transmission	Imidacloprid, dinotefuran	Collar (with flumethrin) Spot-on (alone or with permethrin, permethrin +pyriproxyfen or moxidectin) Oral (tablet)
Oxadiazines	Sodium channel antagonist	INN-Indoxacarb	Spot-on (with permethrin)
Phenylpyrazoles	Binding to chloride channels	Fipronil	Spray Spot-on (alone or with S-methoprene)
Isoxazolines	Binding to chloride channels	Fluralaner, afoxolaner, sarolaner, lotilaner	Oral (chewable) Spot-on Injectable suspension
Bispyrazoles	Inhibition of GABA	Tigolaner	Spot-on (cats only, with praziquantel and emodepside)
Piperidines	Binding to insect/ tick olfactory proteins?	Icaridin (picaridin)	Spray

4.2. Tetracyclic macrolides

Spinosad is composed of the spinosynes A and D (fermentation products of the soil bacterium *Saccharoployspora spinosa*) and is fast, long acting, and highly effective against various insects in agriculture, and against fleas and hard ticks in veterinary medicine (European Medicines Agency, Committee for Veterinary Medicinal Products, 2011). It is also registered for topical administration against human head lice in the US (Parapro, 2025). Acute toxicity is very low in mammals (with the exception of individuals with MDR-1 genetic defects, since spinosad inhibits P-glycoprotein; Sherman et al., 2010). Chronic toxicity has been described in rodents (Santos and Pereira, 2020). Despite being marketed as a “biopesticide” due to its natural occurrence in soil, spinosad is readily absorbed after oral application and subsequently rapidly excreted mainly with the feces (Biopesticides Database, 2025). Thus, environmental contamination is relevant, as it has been shown to impact soil-dwelling invertebrates and is toxic to bees. However, due to rapid degradation in soil its impact on pollinators is generally considered low (Mayes et al., 2003; Dalefield, 2017; Santos and Pereira, 2020; Moreira et al., 2024).

4.3. Carbamates

Propoxur, a synthetic compound with poor solubility in water, is used in different formulations as an insecticide in animals. Its previous registration as household and agricultural pesticide ceased in 2009 (European Commission, 2009). Carbamates reversibly inhibit acetylcholine esterase (AChE), and toxicity (with neurological signs) is usually acute as they can be degraded quickly by AChE itself and can be treated with atropine (Blagburn and Lindsay, 1995). Chronic toxicity has been described in chickens (Rasul and Howell, 1974), whereas dogs do not show chronic intoxication, even after daily application for months (Deplazes et al., 1999). In humans, fatal intoxications have been reported after intentional oral uptake (Pfordt et al., 1987), but general exposure has more recently been linked to male infertility due to their action as endocrine disruptors. This also needs to be considered for the evaluation of other compounds that disrupt the function of ACh (Moreira et al., 2022). After oral or intravenous application, propoxur is metabolized and quickly excreted (mostly as 2-isopropoxyphenol) in urine (National Center for Biotechnology Information, 2025). Similar to pyrethroids, carbamates do not persist in the environment for longer than 12 weeks, with a half-life in soil of around 2–6 weeks (Sun and Lee, 2003). However, they are slightly toxic to fish and aquatic invertebrates, moderately to highly toxic to birds (depending on species), and highly toxic to numerous insects, including bees (Wauchope et al., 1992; Costa, 2014).

4.4. Neonicotinoids

Imidacloprid, nitenpyram, dinotefuran and other neonicotinoids act on the nicotinoid acetylcholine receptors of insects, with a very low affinity for mammalian receptors (Bianciardi, 1997). They are broadly used in crop protection (Jeschke et al., 2011; Giorio et al., 2021) and in veterinary medicine as insecticides in different formulations (ref. Table 2) for the control of fleas and other ectoparasites. Imidacloprid is quickly excreted with urine after uptake by mammals without relevant metabolism (Tao et al., 2019; Wrobel et al., 2022). Acute toxicity in mammals is low (young animals seem to be more susceptible), and clinically resembles nicotine intoxication (Hovda and Hooser, 2002; National Pesticide Information Center, 2023). Imidacloprid is only slightly toxic to fish, but is very toxic to honeybees and other insects, such as ladybirds, as well as to earthworms (Capowiez et al., 2006; National Pesticide Information Center, 2023) and also seems to negatively affect free-living amoebae (Wang et al., 2023). Its toxicity to birds has previously been considered low (Capowiez et al., 2006), but recent work on nest contamination with insecticides showed an increase of unhatched eggs and a tendency for higher chick mortality in relation to imidacloprid contamination of the nests of blue tits and great tits (Tassin de Montaigu et al. 2025). It has been implicated in honeybee mass mortalities that occurred shortly after its introduction as an agricultural pesticide, but unlike fipronil (see below), imidacloprid does not display time-reinforced toxicity in bees. Thus, long-term effects still need to be evaluated. Since 2018, outdoor use of imidacloprid has been banned in the EU (European Commission, 2024), due to its confirmed risk for bees (European Food Safety Authority, 2018). Nevertheless, it is still available in a range of veterinary products in combination with other ectocides and repellents (Table 2). Wastewater is considered a major entry for imidacloprid applied as spot-on ectocide, both from grooming treated dogs and as wash-off from owners' hands after application (Budd et al., 2023; Perkins et al., 2024). In addition, it has been shown that after topical application, imidacloprid can be found in dog's hair for several weeks, so chronic exposure is conceivable for exposed individuals, especially dog owners or veterinarians (Craig et al., 2005). Neonicotinoids applied as seed coating can be found in plant nectar and pollen, but also in honeydew (a product of hemipterans such as aphids that is used as a food source by a large range of other insects), therefore their negative impact on insects is considered to be far reaching (Calvo-Agudo et al., 2019). In addition, due to its long persistence imidacloprid must be expected to have long-term environmental effects, even after its use has been restricted (Fouad and Abdel-Raheem, 2024).

4.5. Oxadiazines

Although indoxacarb, a water-insoluble insecticide, is no longer registered for cockroach control (European Union, 2013), it is still used as a spot-on, in combination with permethrin, for prevention and treatment of flea infestation (Dryden et al., 2013), as an acaricide, and for its anti-feeding effect on sandflies, the vectors of *Leishmania* (Frenais et al., 2014). It has a low to moderate toxicity in mammals due to its highly selective action on sodium channels, which differs from (and complements) that of pyrethroids (Lapied et al., 2001; Zhang et al., 2016). After ingestion, it is quickly absorbed and metabolized and excreted via urine and feces and does not display bioaccumulation. Acute toxicity in mammals results in ataxia, lethargy, tremors, and immobility (Gupta and Doss, 2022b).

Indoxacarb is not readily biodegradable, and is therefore persistent in soil (less so in water) with half-lives, bioavailability and bee toxicity depending strongly on the tested enantiomers (Zhong et al., 2022; Ai et al., 2024). It can also be found in dogs' coats for up to three weeks after application (Gupta and Doss, 2022b). Acute toxicity is high for birds and beneficial insects, and is moderately toxic to fish (Pesticide Properties Database, 2023). Toxicity to snails was demonstrated after exposure to environmentally relevant concentrations (Radwan et al., 2024).

4.6. Phenylpyrazoles

Fipronil was used as an agricultural insecticide in the EU before its ban in 2017 (European Food Safety Agency, 2023) and other countries (Lewis et al., 2016), and for ant control in the USA (Consumer Product Information Database, 2023). In veterinary medicine, it is available for flea control as a spray or spot-on alone or (as a spot-on) in combination with S-methoprene (Lewis et al., 2016). A spot-on combination with permethrin is also available. Dermally applied, fipronil is distributed to the skin and follicle lipids and released to the coat for about four weeks. Oral uptake (e.g., by licking off freshly applied compound) leads to excretion via feces and urine (Gupta and Doss, 2022c). Due to the accumulation in skin and coat (particularly in adipose tissue, primarily as fipronil sulfone; Cravedi et al., 2013), environmental contamination with fipronil contained in hair after topical applications must be considered (Diepens et al., 2023). In addition, studies from the UK demonstrated considerable levels of fipronil in wastewater, likely originating from grooming and bathing dogs, and handwashing pets after application (similar to imidacloprid; see chapter 4.4.) (Budd et al., 2023).

Fipronil persists in soil, with a half-life of around 125 days, but is susceptible to rapid photolysis. Acute and chronic toxicity for mammals (neurotoxicity, thyroid, kidney and liver toxicity) are considered moderate via oral and inhalational routes, and low via the dermal route, with species-specific exceptions. In rats, transplacental transfer of fipronil has been demonstrated (Chang and Tsai, 2020). For birds and beneficial insects, as well as aquatic or soil-dwelling organisms, toxicity is generally considered high (National Pesticide Information Center, 2024).

Fipronil was previously licensed for seed treatment (and this is still the case in non-European countries) and exposure of mammals, including humans, from this source is limited (Lewis et al., 2016). Nevertheless, fipronil can reach flowers and pollen via soil, and bioaccumulation in bees has been considered to be responsible for mass mortalities of bees (Holder et al., 2018). A recent analysis detected fipronil (amongst other insecticides) in nests of blue tits and great tits in the UK, and demonstrated a positive correlation of fipronil concentration with chick mortality (Tassin de Montaigu et al. 2025).

Contamination of chicken feed, and consequently chicken eggs, with fipronil occurred due to the (illegal) combination of fipronil with an otherwise legally marketed product for use in henhouses to combat the poultry red mite in some European countries and Hong Kong in 2017; as a result of this incident, many millions of eggs were destroyed and close to two million laying hens were slaughtered (Nayak et al., 2022; Eissa and Shehata, 2024).

4.7. Isoxazolines

Fluralaner, afoxolaner, sarolaner, and lotilaner are fast-acting and effective against fleas and ticks, as well as follicle and mange mites, by binding to arthropod chlorine channels (Zhou et al., 2022). Fluralaner is 6–28 times more toxic to houseflies than permethrin (Burgess et al. 2020). Despite public and scientific discussions on the side effects of fluralaner, it is generally considered safe to apply these compounds to healthy pets; tolerance in dogs with mdr-1 mutations is considered good (European Agency for the Evaluation of Medicinal Products EMEA, 2015; Gupta and Doss, 2022d). Acute and chronic toxicity are low, with mild, mostly gastrointestinal or, rarely, neurological, signs (Drag et al., 2017; Gupta and Doss, 2022d).

Data on environmental impact are limited to fluralaner, as it is the only isoxazoline that is registered for use on farm animals (chicken) in Europe. It is poorly water soluble, excreted unchanged with feces (and to a small extent urine), and subsequently binds to soil for prolonged periods. Excretion after application is slowed by enterohepatic circulation, contributing to the long efficacy, especially of fluralaner (Committee for Veterinary Medicinal Products, 2017). Elimination in pets seems quicker than in animals with a lower metabolic rate (e.g. wombats; Wilkinson et al., 2021) suggesting that treatment intervals must extended in these cases. Fluralaner is degraded under anaerobic conditions (in water), but persists under aerobic conditions (European Medicines Agency, 2015). Toxicity data suggest significant negative effects on *Daphnia* and honey bees (Committee for Veterinary Medicinal Products, 2017). Excretion of fluralaner by other carnivores can be significantly longer than in domestic cats or dogs, raising concerns about the environmental impact when applied to free-ranging wild carnivores (Berny et al., 2024). In Brazil, fluralaner has recently been registered for ectoparasite control in cattle, and while publications summarize its therapeutic efficacy against ticks, myiasis and horn flies (da Costa et al., 2023; Gallina et al., 2024), they do not mention environmental impact.

4.8. Bispyrazoles

Tigolaner, has been registered in the EU since 2021 in combination with praziquantel and emodepside, two anthelminthic compounds. It inhibits gamma amino butyric acid and is effective against fleas, ticks, and mites. Due to its slow clearance and high volume of distribution, tigolaner has a long-lasting effect with limited accumulation in the licensed dose and application frequency, so even increased doses do not lead to intoxication (Mencke et al., 2023; European Medicine Agency, 2023). Similar to isoxazolines, tigolaner is poorly metabolized and excreted with the feces (European Medicines Agency, 2025d). There are currently no data available on toxicity for invertebrates or to mammals other than cats, where it is low (Mencke et al., 2023).

4.9. Piperidines

Icaridine (picaridine) is a poorly water-soluble compound, not registered as a pharmacotherapeutic compound for animals or humans, but as a biocide for external application as a repellent spray or spot-on with action against insects and ticks. Acute or reproductive toxicity after dermal application, inhalation or oral uptake is practically absent in mammals (Gervais et al., 2009). However, as skin or eye irritation in sensitive individuals has been observed in humans (Tavares et al., 2018) testing for adverse skin reactions should be conducted prior to whole-body application, and care should be taken to avoid eye contact. Toxic effects on amphibia (spotted salamanders) under laboratory conditions have been reported with exposure to concentrations that could, realistically, be present in surface waters (Almeida et al., 2018).

5. Discussion

Current recommendations on the control of ectoparasites and vectors in pets include the regular application of pesticides on animals. Frequently, pet owners utter concerns regarding preventive antiparasitic treatments, especially those against ticks and insects (authors' personal communication, 2025). Besides concerns regarding tolerance, side effects, and an anticipated negative impact on pet health, adverse environmental consequences are also part of the current discussion. These points need to be addressed to maintain owner compliance in parasite control. In particular, ticks and tick-borne diseases are a major contemporary focus of veterinary parasitology, with regular reports on the importance and (danger of) spread of vectors (and, in the case of ticks, longer seasonal activity) and associated pathogens and high rates of infections in questing ticks (Mencke, 2013; Dantas-Torres and Otranto, 2016; Maurelli et al., 2018; Otranto, 2018; Buczek and Buczek, 2020; Zanet et al., 2020; Cunze et al., 2022). Recent publications, however, indicate that environmental pollution with pesticides or parasiticides also impacts on non-target insect diversity, aquatic ecosystems, and other wildlife (Sadaria et al. 2017; Teerlink et al. 2017; Cryder et al. 2019; Foundation for Applied Water Research Stichting Toegepast Onderzoek Waterbeheer, 2019; Guldemond et al., 2019; Sánchez-Bayo and Wyckhuys, 2019; Wagner, 2020; Tassin de Montaigu et al. 2025).

While the negative impacts of pesticides on the environment and non-target organisms are of concern, the existing contamination from agricultural use of pesticides (as discussed recently by Tang et al., 2025) must vastly exceed that of small animal veterinary medicine due to the amounts applied outdoors compared to formulations applied on animals. According to the CVMP comment mentioned above, around 4 tons of imidacloprid were sold as spot-ons and collars in UK (approx. 16.5 mio dogs and cats) in 2017. In the Netherlands (5 mio dogs and cats) around 0.5 tons of phenylpyrazoles against ticks and fleas were sold annually in 2018–2019. However, published amounts for the different compounds used in agriculture vs. veterinary use in Europe were not available to the authors. While the agricultural application of fipronil or imidacloprid in the EU was restricted to indoor and permanent greenhouse use in 2017/2018 (Perkins et al., 2024), since then most EU members approved the emergency use of imidacloprid, which was granted EU-wide in 2021 (Bayer, 2024). Outside of Europe (e.g., in China, Brazil, India, Canada and USA), these compounds are still regularly applied for crop protection (see Bayer, 2024). In USA, fiproles and neonicotinoids are used in agriculture and for urban pest control. Their detection in groundwater seems to depend on land use and geology, factors that also determine the circulation of these chemicals in natural water systems (Goedjen et al., 2024). In general terms, oral, injectable or topical applications in small amounts, like those used for pets, should result in much lower release of chemicals into the environment than from other modes of application (Boxall et al., 2004), and pet (dog and cat) feces contribute a much smaller volume (both per animal and in numbers of animals) compared to large animals, such as domestic equines or livestock, where environmental contamination with parasiticides in feces is a concern (Floate et al., 2005). However, accumulation in certain scenarios, like the mentioned nest building with pet fur, is not easily foreseeable and must be considered in risk assessments. Release of chemicals after application also depends on the application frequency and correct handling, compliance with safety recommendations, mode of disposal of unused compounds etc. To highlight the complex interrelation between insecticide use, environmental pollution, ecological and economic consequences, the fate of the honeybee is often used as an example. Contamination of pollen and other honeybee products with pesticides correlates negatively with colony strength and survival, but pesticide concentration also seems to be correlated with intensive agricultural crop areas. Contamination is mainly linked to fungicides or other chemicals used for crop protection, while insecticides represent only 31 % of the contamination of pollen. So far, no insecticide used for pets has been found in bees or honeybee products, although substances like fipronil and imidacloprid are part of the screening (Barroso et al. 2025). When insecticides such as permethrin have been found in dead honeybee colonies, their detection and concentrations revealed by laboratory investigations suggest that it might have been used for intentionally killing honeybee colonies (Martinello et al., 2021). The circulation of pyrethroids from soil to water or plants is limited due to their strong binding to dirt and the ability of microorganisms to degrade them, which is currently investigated as a method of biodegradation of pyrethroid residues in the environment (Wu et al., 2025).

In addition, chemical compounds applied as drugs are always formulated together with excipients to support the intended pharmacological properties, such as tissue distribution, retention and excretion, and these excipients may also change the chemical properties of the compounds. Although excipients are generally considered environmentally inert, some must be expected to have ecotoxic effects and must be evaluated accordingly (Turek et al., 2023). In addition, formulated compounds can display a higher ecotoxicity than the active compound alone (Cossi et al., 2020) and increase bioavailability (Rozman et al., 2010). Consequently, when evaluating environmental effects of (veterinary) drugs, formulations and not only active ingredients must be considered (Mesnage and Antoniou, 2018; Radwan et al., 2024).

Where applicable, monitoring of environmental samples for parasiticides used in pets must be implemented against this background. The number of doses likely to have been applied (based on sales data) should be considered in the evaluation. Another aspect is the distribution of pesticides after release; agricultural use primarily causes contamination of rural areas, whereas release from use in pets is more relevant for urban and peri-urban areas (Wells and Collins, 2022; Perkins et al., 2024). Risk assessment for different ecosystems is therefore necessary. An evaluation of contamination of ponds in urban settings with and without dog swimming demonstrated higher imidacloprid and fipronil levels in ponds where dog swimming was allowed (Yoder et al. 2024). Since owners questioned in this study were mostly unaware of the problem of water contamination, it appears likely that the recommended waiting times for swimming after application of ectocides are not followed; this has also been indicated in a survey of dog and cat owners in the UK on the use of ectocides (Perkins and Goulson, 2023). Another source of environmental contamination is aquatic pollution derived from wastewater, i.e. handwashing after handling veterinary ectocides (Perkins et al., 2024). The proportion of contamination from these sources still awaits detailed evaluation. For orally applied ectocides, environmental contamination may also arise from lack of compliance of the animals, i.e. tablets or chewables are regurgitated and "released" into the environment without the owners being able to prevent this. Recent research addressing owner views on and challenges of oral medication of their dogs revealed that this type of application, while considered easy to perform at home, poses challenges and can cause concerns and distress (Tarrant et al., 2025). Therefore owner compliance must be considered (and secured) when ectocides are applied this way.

Apart from undesirable, often unforeseen, and in some cases serious, consequences of the release of ectoparasiticides into the environment for non-target animals (and humans), the question whether antiparasitic resistance can be conferred or promoted via environmental compound residues needs to be addressed in detail. Many target parasites of pets, especially fleas or ticks, as well as mosquitoes or nuisance flies, spend considerable times off their host in the environment where they could then be exposed to such residues at low concentrations. It is currently unclear whether and how this could affect the development or phenotypic manifestation of resistance to a single compound, or even a group of compounds. In addition, certain pesticides can co-select for antibiotic resistance in bacteria by promoting antibiotic-resistant strains, e.g. in cases where resistance to pesticides and to antibiotics are genetically encoded nearby on the same genetic elements such as plasmids or share the same mechanisms (e.g. detoxification mechanisms). Evidence for this was presented by increased environmental sampling of resistant bacteria exposed to elevated pesticide concentrations (reviewed by Zhou et al., 2025).

Despite the remaining questions on sources of environmental contamination with insecticides and the missing information on many of the possible consequences, responsible use of veterinary pesticides (both on animals and in the environment for the control of off-host stages, e.g. of fleas) must be strongly advocated by manufacturers and veterinarians (Tarr, 2020). The professionals' (especially the veterinarians') task in this context includes the support of owners' informed decisions on treatment. In addition, recommendations on how to avoid (or at least reduce) environmental contamination before, during, and after application should be provided, both verbally and with written information. This includes correct dosing and application, disposal of leftovers as well as animal excretions and hair that may contain the applied chemicals. The decision to apply antiparasitic compounds should be adapted to the risk of exposure and disease, and should, whenever possible, be accompanied by complementary measures. The advice to owners to collect their pets' feces to prevent the dissemination of fecal pathogens in the environment should be extended to the collection and correct disposal of pet feces (including cat litter!) to avoid the undesirable release of excreted compounds into the environment. According to a German press release of the Süddeutsche Zeitung in 2017, 20 % of the plastic bags with collected dog feces are left behind instead of being disposed for incineration (Hummel, 2017), which not only does not prevent the dissemination of pathogens or chemicals with fecal matter, but add plastic waste to it.

Protocols to obtain targeted environmental data for marketing authorization, as recommended by the EMA and the CVMP, are in place for large animal products and must now be adapted to pets products (European Medicines Agency, 2025b), and such evaluations must also include estimates of release of compounds into the environment both under best practice conditions of recommended application and disposal of residuals and also under conditions of uncontrolled release after improper application and discarding of residuals by animal owners or veterinarians. Estimates of applied amounts of drug and their toxic effects in a defined volume of surface water (Little and Boxall, 2020) are currently oversimplified calculations. Drugs applied on animals are not simply re-distributed into the environment as run-off from animal surfaces; depending on the compound and compound class they are retained for different time periods, excreted via different metabolic pathways, and end up in the environment in different compartments with different retention times depending on stability under environmental conditions.

Feces and urine are the main excreta to be considered for the release of chemicals into the terrestrial environment, and CVMP recommends studying their impact in this framework. As for free roaming cats, the possibilities for control of fecal contamination are limited. However, for dogs, collecting feces to limit spread of infectious agents, especially parasites, is a long-standing recommendation (e.g. in the ESCCAP-guidelines; www.esccap.org), and should immediately be extended to containment of any chemicals released by treated dogs. Canine feces can be collected and incinerated with regular household waste to prevent the spread of unwanted substances and organisms in the environment. However, incineration of municipal waste is not always the standard, and this should be considered as another potential route into the environment for medications. For example, in UK at least 70 % of household waste goes to landfill sites (Waste Managed® UK, 2025) and in several Mediterranean countries and most Eastern European countries, most waste treatment is via landfill, although incineration is increasing (Weghmann, 2023). In USA, although combustion is a primary disposal route for municipal solid waste, a substantial proportion ends up in landfill, with over 146 million tons disposed of by this method in 2018 (United States Environmental Protection Agency, 2023). It must be assumed that such practices can increase the circulation and distribution of undestroyed chemicals released from household waste into the environment, including antiparasitics (as well as other veterinary medication) excreted with previously diligently collected animal feces disposed of as recommended. This is not only important for antiparasitic and antimicrobial substances, but also hormones, anti-cancer drugs, and other bioactive substances (Fent et al., 2006; Jureczko and Kalka, 2020; Okeke et al., 2024). Within the One Health framework, veterinary medicine and human medicine should join forces to protect the environment and to reduce uncontrolled release of any significant chemical from patients. Legal and organizational measures must be taken to address this problem.

Advocating and promoting prudent use of veterinary drugs in general, and weighing the benefits and risks by individually-adapted treatment protocols, will reduce overuse and the associated risks of environmental pollution, as well as the development of antiparasitic resistance, also a topic of increasing concern in small animal parasitology (Bossard et al., 1998; von Samson-Himmelstjerna et al., 2021).

As for the proposed sales regulations (advertisement control and consideration of environmental safety when assigning prescription status), it is suggested to restrict the sale of antiparasitic drugs to veterinary practices or exclusively under veterinary prescription. In addition, veterinarians should apply and promote good practices of responsible use of such compounds, including risk assessments of application, owner instructions on safe use and disposal, raising awareness of potential hazards resulting from incorrect use and disposal - not only to the pet and the owner, but also to the environment. This must also extend to other pet health professionals, such as pet shop owners and pharmacists, as well as pet associations and operators of animal shelters. Consequently, the professional training of veterinarians, veterinary nurses, pet shop owners etc. must include training and information on the correct choice, application and disposal of parasiticides for the prevention of infections in animals. Continuous research is required to evaluate the consequences of drug application, not only to the patient, but also to the environment, and will provide data on risks and benefits.

To further reduce environmental contamination with veterinary ectocides and repellents, recommendations for correct use as described in the product literature (e.g., avoiding washing animals or allowing them to swim in surface water soon after topical product application; correct administration of oral products; correct disposal of used blisters and collars; using disposable gloves when recommended for the application followed by their disposal with solid waste etc.) must be followed and advocated. Owner compliance is key to these measures to reduce the release of products into the environment (Tarr et al., 2020), and professional veterinary support and advice is indispensable to create and maintain this compliance.

The recommendation to refrain from chemical ectoparasite control in pets is not compatible with animal health. Non-medical preventive measures (e.g., regular visual examination for ectoparasites and manual removal; European Scientific Counsel Companion Animal Parasites, 2022) can reduce the infestation of pets by ticks, less so by fleas or dipterans, and is likely not sufficient to prevent transmission of tick-borne pathogens (Leschnik et al., 2013; Probst et al., 2023). In cases where season or locality indicate an increased infestation risk, considerations for applying parasiticides must be taken.

"Alternative" (or, in practice, complementary) control measures for environmental stages of arthropods include biological agents with high specificity, such as the insecticidal (larvicidal) bacterium *Bacillus thuringiensis* for the control of mosquitoes. Due to their selective action against the aquatic larvae of culicids, they can be applied in the environment (Brühl et al., 2020). Environmental stages of ticks can, in principle, be targeted by entomophageous (entomoparasitic) nematodes or fungi, but application is currently limited to small areas and protocols for routine reduction of tick populations do not exist (Lacey et al., 2015; Sullivan et al., 2020; Ebani and Mancianti, 2021; Rajput et al., 2024; Wężyk et al., 2025).

Lack of ectoparasite prophylaxis will increase not only disease risks for pets, but also for zoonotic transmission potential for those pathogens for which pets are reservoirs, e.g. *Leishmania infantum* in dogs (Ribeiro et al., 2013; Courtenay et al., 2019) or *Bartonella henselae* in cats. Weighing the potential health risks against the environmental risks from applying ectocides /repellents is difficult, especially knowing that even should veterinary application be stopped immediately, highly stable compounds would still circulate, and contamination from other sources might continue. Thus, any assessment must seek to answer whether relinquishing (or at least reducing) antiparasitic treatment would make a relevant difference in pollution with these compounds? Recent literature (see above) indicates this is the case, and clear communication from the scientific community to all stakeholders in pet health and the general public on risks and benefits of treatment is especially warranted.

Guidelines for parasite control in pets are based on individual risk assessments in combination with targeted diagnostic measures, and do not promote "indiscriminate use" as some authors describe it (Little and Boxall, 2020). Treatment and treatment frequency of an animal are ultimately the decision of the owner or animal care person. Considering that antiparasitic compounds are drugs, their use must advised and supervised by a veterinarian. However, in many countries ectoparasiticides can be purchased in pet shops, supermarkets, or in the web without prescription, and this situation might promote ectoparasiticide applications outside expert recommendations, leading to undesirable environmental hazards, lack of efficacy, or an unrecognized loss of efficacy, i.e., resistance.

Clearly, the current recommendations of ESCCAP and other scientific panels regarding the antiparasitic treatment of dogs and cats aim to maximize prevention of parasite infections and tick and flea infestations, as well as reduce vector-borne pathogen transmission to pets and humans.

6. Conclusion

Recently, the use of bioactive compounds applied in veterinary medicine for the control of ectoparasites and arthropod vectors has been criticized by ecologists, and many questions revolving around the environmental safety of such applications remain. In the One Health context, we are in need of research to provide evidence-based data on: (a) the extent of release of drugs from any source into the environment compared to other sources; (b) their possible impact(s) on non-target organisms (spanning a broad range from pollinating insects to soil-dwelling invertebrates of various taxa and also free-living vertebrates), and long-term effects on mammals, including humans; (c) the exact sources of environmental contamination with such compounds (specifically, whether they were released pre- or post-intended use, and whether recommendations for handling and disposal were adhered to). Such data will be necessary to determine whether the intentional and correct use of compounds as veterinary drugs is actually the cause of the environmental contamination, as has been indicated in recent publications. Specific actions must the taken to monitor and prevent the release of potentially harmful chemicals at all steps, from production to application, and further down to disposal and waste management. Consequently, recommendations must be formulated based on actual research evidence and not (or not exclusively) on data extrapolated from research on environmental pollution with pesticides in general, and finally, a risk-benefit analysis must support informed decisions on when and how to protect pets from ectoparasites and vector-borne infections.

Finally, "eco-friendly" alternatives for the control of ectoparasites and arthropod vectors must be developed to ensure compatibility (or at least balanced consideration) between animal and human health care, and the protection of the environment. For this, experts in veterinary parasitology must expand their knowledge on the action and side-effects of ectocidal drugs for pets to include the impact of these drugs on the environment. For this they should team up with ecologists and toxicologists for translational research in this increasingly important area.

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CRediT authorship contribution statement

Michael Leschnik: Writing – review & editing, Investigation, Conceptualization. **Robertson Lucy J:** Writing – review & editing, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Anja Joachim:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Wolfgang Bäumer:** Writing – review & editing, Validation, Investigation, Conceptualization. **Ezio Ferroglio:** Writing – review & editing, Investigation, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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